Remarks

Reconsideration of this Application is respectfully requested.

Claims 1-3, 5, 6, 10-13 and 35-49 are pending in the application, with claims 1 and 39 being the independent claims. Claims 1, 10 and 44 are sought to be amended. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

I. Support for Claim Amendments

Support for the amendment to claim 1 can be found throughout the specification, for example, at page 17, line 17 through page 18, line 9, and at page 46, lines 4-26. Support for the amendment to claims 10 and 44 can be found throughout the specification, for example, at page 19, lines 16-26, and in original claim 6.

II. Objection to the Specification

The Examiner indicated that he is unable to locate the abstract for this application. *See* Paper No. 28, page 2. For the Examiner's convenience, a duplicate abstract is being submitted herewith for insertion into the specification.

III. Claim Objections

Claims 36-38 were objected to as being dependent upon a rejected base claim (claim 1). *See* Paper No. 28, page 3. The Examiner indicated that claims 36-38 would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. *See id.* As discussed below, Applicants respectfully traverse the rejections of claim 1. Accordingly, the objection to claims 36-38 as being dependent upon a rejected base claim should be withdrawn.

IV. Claim Rejections Under 35 U.S.C. § 112, First Paragraph

A. Written Description

Claim 1 was rejected under 35 U.S.C. § 112, first paragraph. According to the Examiner:

> The disclosure provides sufficient description of a species of expression of SEQ ID NO: 1. More specifically, the disclosure provides sufficient description for a cDNA designated AD7c-NTP (SEQ ID No: 1) possessing the biological properties when **over-expressed** in neuronal cells. However, the specification does not provide sufficient description of a genus of polynucleotide sequences that possess any of the biological characteristics of SEQ ID No: 1 when the sequence is not over-expressed in said cells.

Paper No. 28, pages 3-4 (emphasis in original). Applicants respectfully traverse this rejection.

The written description requirement of 35 U.S.C. § 112, first paragraph, is fully satisfied for present claim 1. To satisfy the written description requirement an Applicant must convey with reasonable clarity to those skilled in the art that, as of the effective filing

date, the Applicant was in possession of the invention. *See Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1560, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). According to the Federal Circuit, the disclosure of a patent must allow one skilled in the art to visualize or recognize the identity of the subject matter of the claim. *See Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The Federal Circuit has recently indicated that functional descriptions of genetic material may be sufficient to satisfy the written description requirement. *See Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d 1316, 1324 (Fed. Cir. 2002) ("It is not correct, however, that all functional descriptions of genetic material fail to meet the written description requirement.") The principle inquiry is whether the disclosed functional characteristics are coupled with a known or disclosed correlation between function and structure; if so, the written description requirement is satisfied. *See id.* In view of these articulated standards, it must be concluded that the written description requirement is satisfied for Applicants' claim 1.

Applicants first note that claim 1 has been amended to recite "wherein said DNA molecule codes for a protein that has an activity of AD7c-NTP when *over*-expressed in neuronal cells." (Emphasis added). The purpose of this amendment is to make explicit an implicit feature of the invention. Thus, the rejection, insofar as it relates to the recitation of the phrase "said DNA molecule codes for a protein that has an activity of AD7c-NTP when *expressed* in neuronal cells," has been fully accommodated.

Moreover, Applicants have provided in the specification a detailed analysis of the sequence characteristics of the AD7c-NTP cDNA and of the corresponding translated amino acid sequence. *See* specification at page 34, line 6, through page 35, line 28. Applicants have also described various activities possessed by proteins encoded by AD7c-NTP and

methods for assaying such activities. *See, e.g.*, specification at page 46, lines 4-26. In addition, methods for making DNA molecules that are 90% homologous to a reference DNA molecule are common in the field of molecular biology and are also described in the specification. *See, e.g.*, specification at page 19, lines 3-15. In view of these factors, a skilled artisan would be able to clearly visualize and recognize the DNA molecules encompassed by claim 1.

Furthermore, the claim itself recites a correlation between the structure and function of the DNA constructs encompassed thereby. The claim specifies that the DNA molecule of SEQ ID NO:1 or a DNA molecule which is at least 90% homologous thereto "codes for a protein that has an activity of AD7c-NTP when over-expressed in neuronal cells." Therefore, the written description requirement is satisfied for claim 1.

As the above discussion demonstrates, the standards articulated by the Federal Circuit compel the conclusion that the written description requirement is satisfied for claim 1. The guidelines set forth by the USPTO also compel the same conclusion. As noted in Applicants' previous response, the USPTO's Synopsis of Application of Written Description Guidelines (hereinafter "Written Description Synopsis") specifically supports Applicants' assertion that the subject matter of claim 1 is adequately described in the specification.

Briefly, Example 14 of the Written Description Synopsis sets forth an analysis of the written description for a claim directed to "[a] protein having SEQ ID NO:3 and variants thereof that are at least 95% identical to SEQ ID NO:3 and catalyze the reaction A→B." Written Description Synopsis at 53. It is concluded in Example 14 that the written description requirement is satisfied because: (1) the claim specifies that the variants encompassed thereby must have a particular activity and must be 95% identical to SEQ ID

NO:3; (2) there is an actual reduction to practice of the single disclosed species; (3) procedures for making variants of SEQ ID NO:3 which have 95% identity to SEQ ID NO:3 and retain its activity are conventional in the art; and (4) the specification describes an assay that can be used to identify other proteins having the claimed catalytic activity. *See* Written Description Synopsis at 53-55.

When applied to claim 1, the rationale set forth in Example 14 of the Written Description Synopsis compels the conclusion that the written description requirement is fully satisfied with respect to Applicants' claim 1. First, current claim 1 specifies a DNA molecule which is at least 90% homologous to SEQ ID NO:1 and which codes for a protein that has an activity of AD7c-NTP when over-expressed in neuronal cells. Second, there has been a reduction to practice of a DNA molecule having SEQ ID NO:1. Third, procedures for isolating nucleic acid molecules that are at least 90% homologous to SEQ ID NO:1 are described in the specification and are well-known in the art. Fourth, assays are described in the specification which will identify other DNA molecules encoding proteins having an activity of AD7c-NTP. *See* Applicants' Amendment and Reply filed July 9, 2002, pages 11-13. Therefore, the factors which lead to the conclusion that the written description requirement is satisfied in Example 14 are also found for the subject matter of claim 1. The USPTO's Written Description Synopsis necessarily leads to the conclusion that the written description requirement is fully satisfied for present claim 1.

In summary, based on Federal Circuit precedent and the guidance provided by the USPTO, there is adequate written description for the subject matter of claim 1. Accordingly, Applicants respectfully request that the rejection of claim 1 under 35 USC § 112, first paragraph, for insufficient written description, be reconsidered and withdrawn.

B. Enablement

Claims 1-3, 5, 6, 10-13, 35-38 and 44-47 were rejected under 35 U.S.C. § 112, first paragraph, because, according to the Examiner, "[t]he specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims." Paper No. 28, page 8. Applicants respectfully traverse the rejection.

1. Claim 1 Has Been Amended to Recite "Over-Expressed"

The Examiner stated,

> the as-filed specification provides sufficient guidance for SEQ ID NO: 1 when SEQ ID NO: 1 is over-expressed in neuronal cells. However, the as-filed specification does not provide sufficient guidance for the genus of nucleotide sequences that has an activity of AD7c-NTP when **expressed** in neuronal cells.

Paper No. 28, page 11 (emphasis in original).

Although Applicants respectfully disagree with this assessment, claim 1 has nonetheless been amended to recite "wherein said DNA molecule codes for a protein that has an activity of AD7c-NTP when *over*-expressed in neuronal cells." (Emphasis added). The purpose of this amendment is to make explicit an implicit feature of the invention. Thus, the rejection, insofar as it relates to the recitation of the phrase "said DNA molecule codes for a protein that has an activity of AD7c-NTP when *expressed* in neuronal cells," has been fully accommodated.

2. The Invention is Adequately Described in the Specification

The Examiner also stated, "since the claimed invention is not supported by sufficient description . . . one skilled in the art would not have known how to make and use the claimed invention so that it would operate as intended. . ." Paper No. 28, page 8. As discussed in detail above, and in Applicants' previous response, the specification provides sufficient description of the invention encompassed by the present claims. Thus, the rejection for lack of enablement cannot properly be based on the alleged insufficiency of the description of the invention.

3. It Would Have Required Only Routine Experimentation to Obtain a DNA Molecule Which is At Least 90% Homologous to SEQ ID NO:1 and Which Has an Activity of AD7c-NTP When Over-Expressed In Neuronal Cells

In order to satisfy the enablement requirement of 35 USC § 112, first paragraph, the claimed invention must be enabled so that any person skilled in the art can make and use the invention without undue experimentation. *See In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). The Examiner stated that a person of ordinary skill in the art "would be able to determine a DNA sequence with 90 percent identity to SEQ ID No: 1," but that "it is not apparent to one skilled in the art if the nucleic acid sequence with at least 90 percent homology to SEQ ID No: 1, would exhibit the same biological function of SEQ ID No: 1." Paper No. 28, page 8. This conclusion is based on the supposed unpredictability between "a sequence of a peptide and its tertiary structure (i.e. its activity)." *Id.* As discussed below, a person of ordinary skill in the art would be able to make, use and practice the compositions and methods of the present invention without the need to predict tertiary

structure or activity from peptide sequence information. Thus, obtaining DNA molecules for use with the present invention would not entail undue experimentation.

At the time the present invention was made, persons of ordinary skill in the art could have easily obtained DNA molecules for use with the present invention by: (1) obtaining DNA molecules that are at least 90% homologous to SEQ ID NO:1, and (2) assaying the corresponding proteins for an activity of AD7c-NTP when over-expressed in neuronal cells. As acknowledged by the Examiner, one of ordinary skill in the art would have been able to obtain DNA molecules that are at least 90% homologous to SEQ ID NO:1 using only routine methods in the art. *See, e.g.*, specification at page 19, lines 3-15. In addition, it would have required no more than routine experimentation to assay the corresponding proteins for an activity of AD7c-NTP when over-expressed in neuronal cells. The specification describes various methods for assaying AD7c-NTP activity. For example, transgenic animals can be made that over-express AD7c-NTP, and, once obtained, the transgenic animals may be analyzed for evidence of neuronal or neuritic abnormalities associated with Alzheimer's disease, neuroectodermal tumors, malignant astrocytomas and glioblastomas. *See* specification at page 20, lines 1-29. Additionally, *in vitro* methods can be used which involve the overexpression of AD7c-NTP in neuronal cells and the subsequent analysis for cellular characteristics of Alzheimer's disease, including apoptosis and neuritic sprouting. *See* specification at page 46, lines 4-26.

Since a person of ordinary skill in the art, based on the present specification, would have easily been able to obtain DNA molecules that are at least 90% homologous to SEQ ID NO:1, and assay the corresponding proteins for an activity of AD7c-NTP when over-

expressed in neuronal cells, it cannot be concluded that obtaining DNA molecules for use with the present invention would involve undue experimentation.

4. Claims 10 and 44 are Fully Enabled

The Examiner also stated, "with respect to the *in vitro* methods contemplated in claims 10 and 44, the as-filed specification only provides sufficient guidance for one skilled in the art to use neuronal cells and not the full breadth of host cells encompassed by the claims." Paper No. 28, page 9. The Examiner also stated "the claim encompasses an *in vitro* method, however step [sic] (iii) in part b) of the claims read on an *in vivo* method."

Applicants note that, in claims 10 and 44, non-neuronal host cells can be used to detect: (i) the suppression or prevention of expression of the protein coded for by the DNA construct of said host cell; and (ii) the increased degradation of the protein coded for by the DNA construct of said host cell. That is, the suppression or prevention of expression of the protein, and the increased degradation of the protein, can be detected in numerous types of host cells besides neuronal cells. *See, e.g.*, specification at page 19, lines 16-26, and at page 22, line 24 through page 25, line 23 (describing exemplary methods for assaying NTP expression that do not necessarily require the use of neuronal cells). Candidate drugs that cause the suppression or prevention of expression of the protein, or that cause the increased degradation of the protein -- *in any type of host cell* -- are candidate drugs that are potentially useful for the treatment or prevention of Alzheimer's disease, neuroectodermal tumors, malignant astrocytomas and glioblastomas.

Claims 10 and 44 also include detecting: (iii) the reduction of frequency of at least one of neuritic sprouting, nerve cell death, degenerating neurons, neurofibrillary tangles or

irregular swollen neurites. Applicants submit such "detecting" implicitly involves the use of neuronal cells. In order to make this aspect of the claims explicit, Applicants have amended claims 10 and 44 to recite "(iii) the reduction of frequency of at least one of . . . in said host cell, wherein said host cell is a neuronal cell." Thus, the Examiner's comments regarding the use of non-neuronal host cells in detecting the reduction of frequency of at least one of neuritic sprouting, nerve cell death, degenerating neurons, neurofibrillary tangles or irregular swollen neurites, has been fully accommodated.

In view of the foregoing remarks, Applicants submit that a person of ordinary skill in the art would be able to make, use and practice the compositions and methods of the present invention using only routine experimentation in the art. Accordingly, Applicants respectfully request that the rejection of claims 1-3, 5, 6, 10-13, 35-38 and 44-47 under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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Version with markings to show changes made

Please substitute the following claim 1 for the pending claim 1:

1. (Thrice amended) A DNA construct, which comprises a DNA molecule of SEQ ID NO:1 or a DNA molecule which is at least 90% homologous thereto, wherein said DNA molecule is under control of a heterologous neuro-specific promoter, and wherein said DNA molecule codes for a protein that has an activity of AD7c-NTP when over-expressed in neuronal cells.

Please substitute the following claim 10 for the pending claim 10:

10. (Twice Amended) An *in vitro* method for screening a candidate drug that is potentially useful for the treatment or prevention of Alzheimer's disease, neuroectodermal tumors, malignant astrocytomas, and glioblastomas, [which comprises] said method comprising:

(a) contacting a candidate drug with the host cell of claim 5, and

(b) detecting at least one of the following:

(i) the suppression or prevention of expression of the protein coded for by the DNA construct of said host cell;

(ii) the increased degradation of the protein coded for by the DNA construct of said host cell; or

(iii) the reduction of frequency of at least one of neuritic sprouting, nerve cell death, degenerating neurons, neurofibrillary tangles, or irregular swollen neurites and axons in [the host] said host cell, wherein said host cell is a neuronal cell;

due to the drug candidate compared to a control cell line which has not contacted the candidate drug.

Please substitute the following claim 44 for the pending claim 44:

44. (Once amended) An *in vitro* method for screening a candidate drug that is potentially useful for the treatment or prevention of Alzheimer's disease, neuroectodermal tumors, malignant astrocytomas, and glioblastomas, [which comprises] said method comprising:

(a) contacting a candidate drug with the host cell of claim 42, and

(b) detecting at least one of the following:

(i) the suppression or prevention of expression of the protein coded for by the DNA construct of said host cell;

(ii) the increased degradation of the protein coded for by the DNA construct of said host cell; or

(iii) the reduction of frequency of at least one of neuritic sprouting, nerve cell death, degenerating neurons, neurofibrillary tangles, or irregular swollen neurites and axons in [the host] said host cell, wherein said host cell is a neuronal cell;

due to the drug candidate compared to a control cell line which has not contacted the candidate drug.